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Multifunctional actives for oily skin and scalp disorders

Though the conventional hair care market is a mature one, there are still many opportunities to innovate and radicalise this sector. As the needs of consumers are becoming more complex, the corresponding products evolve towards more sophisticated and solution-oriented concepts by default. Just in the first of half of 2014, 72% of global hair care launched had a 'beauty enhancing' claim. Between 2009 and 2014, there were almost 10,000 product launches that addressed oily skin and oily hair concerns. Shampoos continue to dominate the innovations in hair care in 2014 accounting for more than one third of total launches. Looking at new claims such as 'brightening/ illuminating' in the hair care products, we learn that not only the hair care market is following the trends of skin care innovations but also is looking towards more positive functional attributes rather than damage reversal and protection.[1]

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Based on the data extracted through Mintel, hair care products need to become more segmented not just by hair type but also separated by scalp type with specific formulations for oily scalp and dry scalp. The US alone provided an estimated $5.05 billion dollar shampoo and conditioner market and is projected to grow steadily over the next four years and reach a value of $5.6 bn by 2017.[1] However this growth will likely be driven by the development of new formats and skin care-inspired trends for hair care.[1] Multifunctional claims that bring solutions to several ongoing and interrelated concerns are gaining traction in the US market and driving the growth.

Interestingly, the emerging economies of India and Indonesia offer rapidly developing shampoo and conditioner segments versus the more mature markets such as Japan, France and Italy.[1] However scalp care is of extreme importance particularly in Asia where the number of scalp related issues is on the rise. In China, for example, 68% of the consumers suffer from dandruff, 67% have itchy scalp and 56% are afflicted with oily hair/scalp.[2] In 2014, almost one-fifth of the products were formulated for consumers with skin disorders.

The men's market is a relatively underserved one. Men often do not perceive the additional benefits of using different shampoo and conditioners. This is also due to the fact that most of the men's products were solely focused on dandruff control. In recent years, men have shown a willingness to pay a premium for products that bring additional value;[1] multifunctionality being considered a real benefit for these consumers.

The Mintel database reveals that almost 8,000 launches between 2009 and 2014 carried the claims of addressing 'oily skin'. The same research for 'oily scalp' remedies revealed 150 launches in those years. Once the two claims of 'oily hair' and 'oily skin' are juxtaposed, the number of the launches dwindles down to two products. Meanwhile, over 1,800 products were launched to address 'oily hair' concerns.

Most of these products are formulated with a wide range of botanicals varying from mostly lemon and citrus to nettle, rose and menthol. The claim of oily hair is often combined with anti-dandruff, pH-neutral and anti-inflammatory ingredients or salicylic acid and zinc pyrithione. There were also many other products that have added additional oils to help break the cycle of the skin's need to over-produce sebum. Others claim to have oil added or mineral and vitamin fortified to restore the normal conditions to both hair and scalp. Among these, there were a few dry shampoos that utilised zea mays starch or natural clay to simply soak up the oil. However, very few products launched during the past five years contain ingredients that address the root cause of the sebum over-production.

The physiological role of sebum for skin and scalp

Sebum production has an important function in barrier protection and trans-epidermal water loss (TEWL). Human sebum produced by sebocytes is composed of triglycerides, saturated and unsaturated fatty acids, wax esters, sterol esters, cholesterol, cholesterol esters, and squalene.[3] Epidermis keratinocytes produce ceramides, cholesterol and free fatty acids.[4,5] Once the triglycerides are hydrolysed, they then release glycerol, which is an important factor that supports skin elasticity, hydration of the *stratum corneum* and barrier repair. Sebum in hair lubricates both scalp and hair thus reducing its friction. It also brings dead skin cells in the follicle up to the surface. Sometimes due to hormonal changes, genetics, poor nutrition or environmental stress, sebaceous glands may overproduce

sebum. This can result in oily scalp and hair as well as acne and hair loss conditions.

Although oily/hair scalp is considered a cosmetic problem and not a dermatological condition, the absence of adequate scalp care treatment to treat oily scalp disorder, could lead to serious scalp pathology (dandruff, seborrheic dermatitis, alopecia).[6] Clinical literature provides evidence that the occurrence of such pathologic skin conditions negatively impact individuals' quality of life.[7,8] These pathologies provoke deleterious psychosocial impact on human self-esteem and a healthy self-image.

The oily appearance of scalp is due to an accumulation of sebum on the scalp as a consequence of an excess sebum excretion by sebaceous glands.[9,10] The accumulated 'sebum' on the scalp surface is a mixture of sebum produced by sebaceous glands and lipids produced by keratinocytes. This epidermal lipid is very important to skin's hydration. If this component is disturbed or stripped off though use of harsh detergents, skin's permeability barrier may become compromised allowing excessive water loss, and as a result of this increase in trans-epidermal water loss the skin and scalp will face dryness.[35] The water contents of the *stratum corneum* of healthy skin must be greater than 10% and the skin's lipidic component plays an essential role in maintaining a balanced ecosystem.

The skin surface of oily skin and scalp is often characterised by an abnormal lipid composition (decrease in ceramides and sphingolipids content).[11] These abnormalities in lipid composition are linked to hyperkeratosis, barrier dysfunction, and weakness of the cell follicle membrane. Consequentially, the weakness of the cell follicle membrane induces the release of digested lipids, which in turn, increase the amount of superficial sebum. Once excreted, the accumulated sebum is spread over the scalp surface and on hair giving it an oily appearance.

The normal scalp has a biotic commensal community (*Staphylococcus* spp., *Propionibacterium* spp., and *Malassezia* spp.)[12] On the dandruff-afflicted scalp, the levels of *Malassezia* increase by 1.5 to 2 times their normal level.[13] The presence of these microorganisms (*Malassezia restrica*, *Malassezia furfur* and *Malassezia globossa*)[14] on the oily scalp provide an ideal medium (inflammatory, irritant) which leads to the development of dandruff and/or seborrheic dermatitis.[15] The sebum is degraded by oxygen and microorganisms found on the scalp surface. Once degraded the sebum becomes cytotoxic and irritant due to free fatty acid liberation, thus provoking reactive follicular hyperkeratosis and epidermis alteration marking the onset of scalp disease.

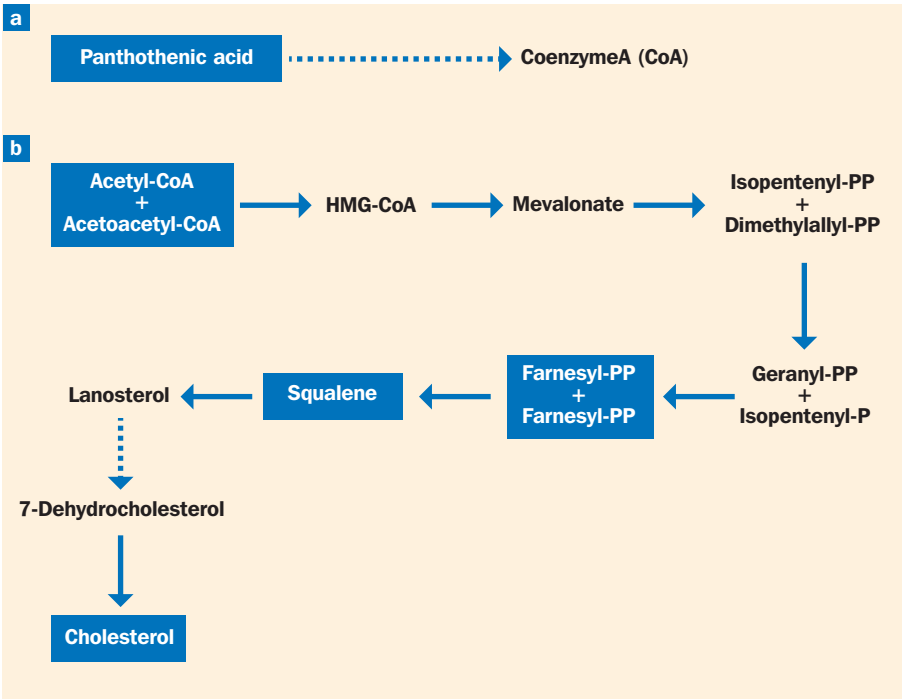

Figure 1: *The biosynthesis of Coenzyme A and cholesterol.*

Regulating sebum production with a selected mix of multifunctional ingredients

In this study, we assessed the efficiency of active ingredients (panthenyl triacetate, farnesol, farnesyl acetate) to treat the metabolic origin of scalp disorder by limiting the excretion of sebum at the scalp surface via the modulation of the lipid metabolism process involved in sebaceous gland and in the epidermis.

Concept of this selected mix

Panthenyl triacetate (PTA), farnesol, and farnesyl acetate (FA) were selected for their biological properties. Panthenyl triacetate and farnesyl acetate were respectively synthesised by acetylation of panthenol and farnesol. Panthenol and panthenol derivative (PTA) are converted into pantothenic acid *in vivo*.[16] Pantothenic acid is categorised as part of the vitamin B complex family and is a characteristic natural by-product of the human metabolism. Pantothenic acid is one of several precursor substances forming coenzyme A,[17] which is an important cofactor for acylation reactions in numerous biochemical processes in the body. Coenzyme A also plays a decisive part in the cholesterol synthesis (Fig. 1).

Farnesol and farnesol derivatives (FA) are natural substances of high biological potency, which are also found in this form as bioactivators in human skin. Farnesol and farnesol derivatives are widespread in the plant world, in particular in the essential oil plant. The derivatives of panthenol and farnesol were used in order to provide a sustained action. Indeed, their conversion is slower in comparison to panthenol and farnesol into biologically active molecules.

The scalp microorganisms are known to have a limited growth due to the intrinsic antifungal and antibacterial properties of the three active ingredients, panthenyl triacetate, farnesol and farnesol acetate, used in the cosmetic formula. By using the cosmetic formulation, the quality of sebum composition is controlled (by panthenyl triacetate, farnesyl acetate and farnesol) and protected against microorganisms and oxidation.

Clinical investigations

Material and methods

Cream and shampoo formulas

The active ingredients were used in the cream at 5% and in the shampoo at 2%, with the following formulas:

- *INCI composition of the cream containing the active ingredient Unitrienol T-27 at 5%*: Water, Caprylic/Capric Triglyceride, Beeswax, Lanolin Corona, Safflower Oil, Decyl Oleate, Unitrienol T-27, Sorbitan Sesquioleate, Cholesterol, Trilaurin, Uniphen P-23 (Preservative), Perfume.
- *INCI composition of placebo cream*: Water, Caprylic/Capric Triglyceride, Beeswax, Lanolin Corona, Safflower Oil, Decyl Oleate, Sorbitan Sesquioleate, Cholesterol, Trilaurin, Uniphen P-23 (Preservative), Perfume.

- *INCI composition of the shampoo containing the active ingredient Unitrienol 7-27 at 2%*: Water, Sodium Laureth Sulfate, Sodium Lauryl Sarcosinate, Decylglucose, Natrium Hydroxide, Cocamidopropylbetain, PEG 40 Hydr. Castor Oil, Unitrienol T-27, Carbopol ETD 2020, Unigerm G-2, Polyquaternium-10, Perfume.
- *INCI composition of the placebo shampoo*: Water, Sodium Laureth Sulfate, Sodium Lauryl Sarcosinate, Decylglucose, Natrium Hydroxide, Cocamidopropylbetain, Peg 40 Hydr. Castor Oil, Carbopol ETD 2020, Unigerm G-2, Polyquaternium-10, Perfume.

Sebum investigation on human skin: forehead test method

The quantity of sebaceous matter on the skin surface was measured using a sebumeter in accordance with the method developed by H. Schaefer and H. Kuhn-Bussius.[38] The principle of the method is based on the fact that when roughened glass or roughened plastic film is pressed against the skin it absorbs grease from the latter and thereby becoming transparent. The degree of transparency depends on the amount of grease on the skin and is measured photometrically. The sebumeter is in principle a 'grease spot' photometer. By pressing a matte plastic strip against the skin some of the latter's grease is taken up and can be photometrically measured by the brightening effect it produces on the roughened glass.

Panel description and test procedure

Twenty subjects (10 men and 10 women) under 30 years of age with predominantly seborrheic skin or mixed to greasy skin were included in the study. The subjects treated their skin with the cream containing the active ingredient twice a day over 45 days and then stopped its use in the five subsequent weeks. The skin grease level was measured on the forehead about 2 cm above the nose. Individual measurements were made at intervals of approximately 10 days, and no cream being used the day before the measurement and on the evaluation day.

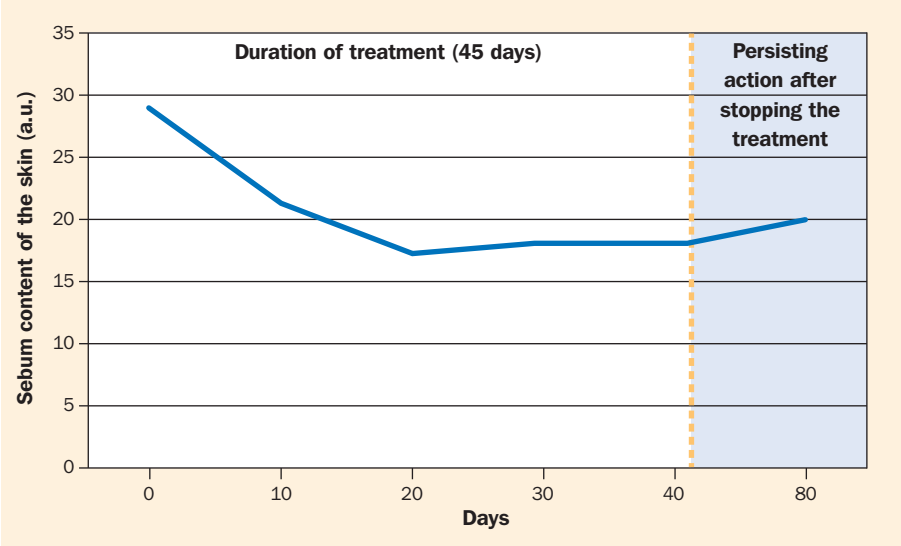

Figure 2: *Content of sebaceous matter in the skin after application of a cosmetic cream containing the active ingredient (sebumeter analysis).*

Sebum investigation on human hair and human scalp: test method of assessment of the oily hair grade

The assessment of the efficacy of the shampoo was based on a clinical scoring of the 'oily aspect of the hair roots' according to a 7-grade scale (from R0 to R6). The grade R0 corresponds to 'no oily' aspect and the grade R6 correspond to 'very oily aspect'. The scoring was performed at D0, D14, D28, and D35. The data were analysed according to the percentage of reduction of the clinical scoring retrieved at each study time.

Quantitative sebumetric analysis was also performed on the forehead skin (median area at the hairline) and on the scalp of the volunteers with the Sebumeter SM 815 (Courage & Khazaka) at the beginning of the study (D0), after 14 days of useand after 28 days of use of the tested product .

Another measurement was taken on D35, 7 days after stopping the treatment (use of their usual product). For each time (D0, D14, D28 and D35), three measurements were taken on the median forehead skin (median area at the hairline). The average and standard deviation of these three values was calculated and kept as the experimental value.

Panel description and test procedure

Twenty-eight healthy women and men adult volunteers with oily hair and scalp skin, ages ranging from 22 to 68 years old, with a mean sebum rate >80 μg/cm^2 were included in the study. Among 28 subjects, 14 used either shampoo with active ingredients or placebo for 28 days. Then they used their usual shampoo from D28 to D35. They were asked to use the shampoo 3 or 4 times per week on wet hair, to massage gently to lather and then rinsed off. Before each visit to the laboratory (D14, D28, D35), volunteers were required to wash their hair on the previous morning. The volunteers, using a questionnaire, assessed the cosmetic performance of the shampoo.

Results and discussion of the clinical assessments

During the clinical evaluation, the use of the cream containing the active ingredients (farnesol, farnesyl acetate and panthenyl triacetate) applied on a greasy forehead has decreased the sebum content by about 40% after 30 days of treatment (Table 1) achieving a rate generally corresponding to that of normal skin. The sebum reduction observed persists also after cessation of the treatment (Fig. 2), showing the long lasting effect of the mix of the active ingredients.

The reduction of oily roots on the scalp was expected to be more difficult, as the active ingredients were formulated in a rinse-off formula (shampoo) with a short contact time with the scalp (estimated to be between 30 seconds to 2 minutes).

Table 1: Content of sebaceous matter in the skin after application of a cosmetic cream containing the active ingredient and % of decrease in comparison to day 0.

Time	Sebum quantity (mean±standard	Average variation (%) *vs.* T0 (sebumeter analysis)
Day 0	28.87±7.9	
After 10 days	21.3±7.4	–26.00
After 20 days	17.4±5.1	–39.00
After 30 days	18.36±6.2	–36.00
After 45 days	18.26±5.9	–36.8
After 80 days	19.92±6.3	–44.8

When applied on the oily scalp in a shampoo formula, this mix surprisingly delivered excellent results. A minus 40% reduction of the oily hair roots has been observed after 28 days of treatment (Table 2), with an extended benefit when the volunteers stopped using this specific shampoo to use again their traditional shampoo (Fig. 3).

For both applications (oily skin or oily scalp), the efficiency of the treatment was seen in quasi all subjects (20 and 13 respectively for the forehead panel and for the hair panel).

Scalp sebum has dual properties (protection against itching and/or induction of itching) depending on its quality and quantity.[18,19] Several authors have demonstrated that chemical composition of skin surface lipids is severely altered in different skin diseases such as atopic dermatitis, seborrheic dermatitis and psoriasis.[20,21] Whereas, sebum content was significantly lower in people with sensitive scalp to hair dyes compared to non-sensitive group.[19] Based on these data, we can think that there is an absolute need to control the quality and quantity of the sebum excreted by using specific scalp care treatment to avoid the future development of scalp disease or discomfort.

We have previously shown that panthenol and panthenol triacetate induced a modulation of lipids metabolism and particularly in cholesterol metabolism.[16] The cholesterol is involved in epidermis differentiation leading to a better barrier function. It was demonstrated that panthenol enhances skin barrier repair.[22,23] The sebum quality is probably also modulated by farnesol and farnesol derivatives since these compounds are constituents of squalene[24] and cholesterol[25,26] biosynthesis in the skin.

Modulation of squalene, cholesterol and ceramides biosynthesis by panthenol derivatives and farnesol derivatives leads to the improvement of the weakness of the cell follicle membrane occurring in some skin pathologies (acne, dermatitis seborrheic). The rupture of a weak cell follicle membrane is responsible in part for the increased sebum excretion.

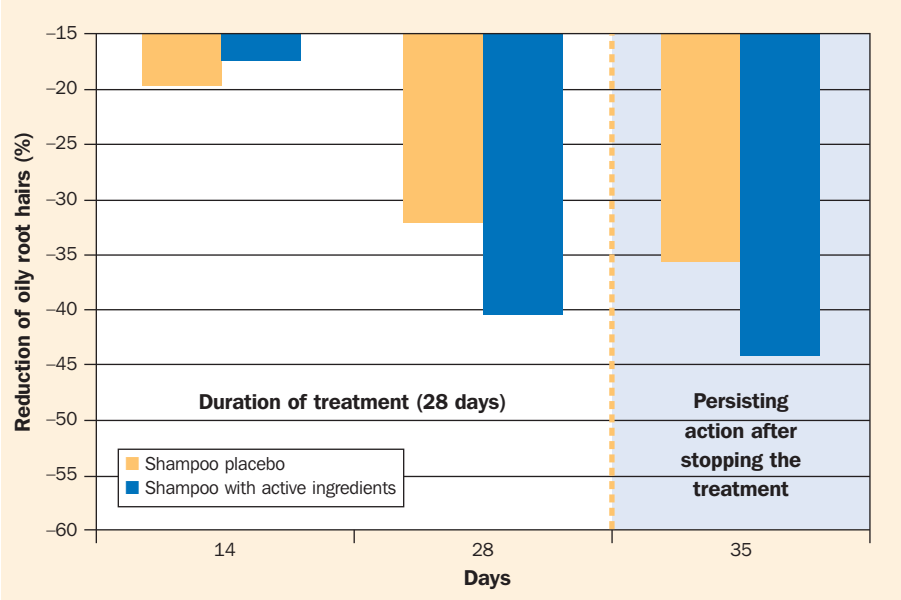

Figure 3: *Percentage of reduction of oily hair roots after application of a shampoo containing the active ingredients (Based on clinical scoring analysis).*

During this study we also tried to measure the sebum quantity by sebumeter directly on the scalp and on the forehead skin at the hairline. The results obtained were aberrant with no correlation with the clinical scoring seen and the volunteer's satisfaction (Fig. 4).

It is well recognised that degradation of sebaceous secretions (by microorganisms) results in inflammation, irritation, itching and scalp flaking.[27] In order to stop the modification of sebaceous secretion by microflora, we developed a cosmetic composition containing farnesol and farnesol derivatives for their anti-microbiological properties for scalp care. Studies have shown that farnesol affects the resistance of bacteria such as those in *Staphylococcus aureus* biofilms[28,29] and fungi (*Candida dubliniensis* strains).[30] Farnesol inhibited also the development of fluconazole resistance seen in *Candida albicans*.[31]

Additionally, this combination of active ingredients possesses anti-inflammatory and antioxidant properties needed for the limitation of irritation and scalp itching.

The anti-inflammatory property is due to panthenyl triacetate,[22,32] farnesol and its derivatives[33] whereas the antioxidant properties are provided by farnesol.[34] Tocopherol is an antioxidant found naturally in skin, and is provided through nutrition. Skin tocopherol is transported by sebum to the skin surface.[35-37] During inflammatory and oxidative conditions the naturally inherent tocopherol is depleted.[35] Once depleted from tocopherol, the sebum remains unprotected becoming a target for oxidation, thus maintaining this deleterious vicious circle: lipids oxidation leading to lipids degradation, which creates a sensitive and irritated scalp. Due to farnesol content of the scalp care formulation, a topical sebum protection is also awarded.

Table 2: Clinical scoring of oily aspect of the hair roots.

Time	Clinical scoring of oily aspect of the hair (mean±standard deviation)		Average variation (%) *vs.* T0	
	Shampoo with active ingredients	Shampoo placebo	Shampoo with active ingredients	Shampoo placebo
Day 0	4±1	4±0.96		
After 14 days	3.31±1.32	3.21±0.97	–17.30	–19.60
After 28 days	2.38±1.19	2.71±0.79	–40.40	–32.10
After 35 days	2.23±1.09	2.57±1.09	–44.20	–35.70

Conclusion

We have demonstrated that a selected mix containing farnesol, farnesyl acetate and panthenyl triacetate (used as a cream or a shampoo) is effective in treatment of oily scalp and oily skin with the same level of efficacy and persistency. The skin sebum content was decreased and the clinical investigations revealed long lasting effect after cessation of the treatment. The intrinsic and synergic multi properties (metabolic stimulators, antimicrobial agent, anti-inflammatory agents) of active ingredients contained in the scalp care treatment are of great interest to treat scalp disorders (irritated scalp, dandruff, seborhheic dermatitis).

The number of product launches that provides a solution to the duality of oily hair and skin reveals that with two products launched in the past five years and the narrow range of ingredients that lack targeting the biological pathways and root cause of the sebum over-production, there is a void for an effective remedy. Taking inspiration from skin care and designing

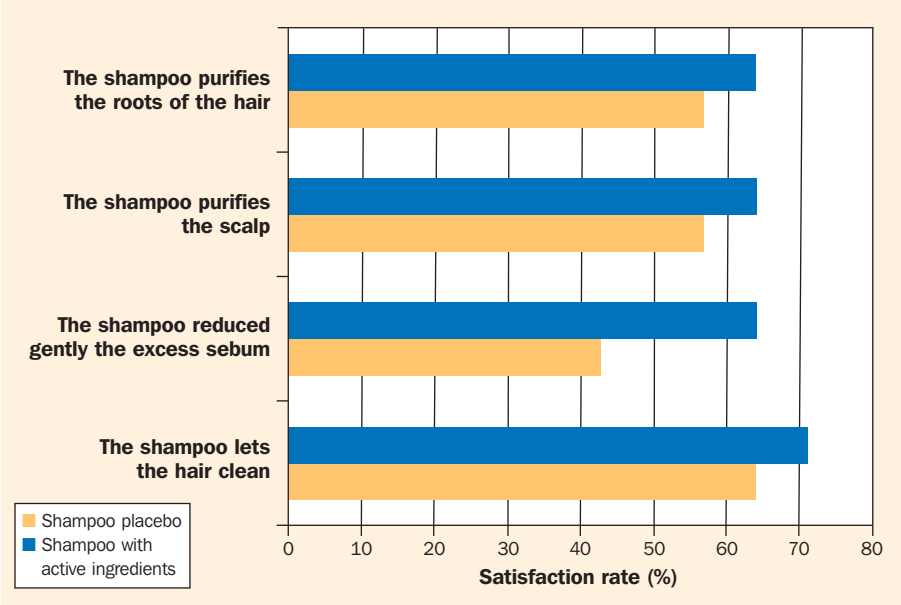

Figure 4: *Volunteers' satisfaction rate (Questionnaire analysis).*

products that are specific to the skin type as well as the hair type rather than the traditional hair types only, may provide a global solution for consumers. PC

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